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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,473	11/13/2007	Xian-Ming Zeng	TEVE-124US	9501

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EXAMINER	
SINGH, RANDEEP	
ART UNIT	PAPER NUMBER
1615	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,473	ZENG ET AL.	
	Examiner	Art Unit	
	RANDEEP SINGH	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-12* is/are pending in the application.

5a) Of the above claim(s) *1-10* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-10* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Applicants' Response dated 10/21/2011 has been entered and carefully considered. In Applicants' Response, claims 6, 9 and 11 were amended. Claims 1-10 are pending and have been examined in this action. Claims 1-10 remain rejected.

Previous Rejections

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are maintained. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Bystrom et al. (hereinafter "Bystrom").

Regarding claim 1, Bystrom discloses a process for preparing a medicament comprising combining a pharmaceutically active ingredient in the form of an agglomerate of primary particles having an agglomerate particle size such that the agglomerate is capable of passing through a sieve having a mesh of 50-3000 microns with a pharmaceutically acceptable carrier (see column 5, lines 3-23 and column 4, lines 30-65). The processes disclosed in Bystrom further include passing the powder through a sieve or deagglomerating the powder in an inhaler to obtain particles within a respirable particle size range (see column 5, lines 21-23 and column 5, lines 56-63). The powder of Bystrom consists of particles having a diameter of less than 10 microns (see column 4, lines 20-24). Preferably, at least 90% of the powder consists of particles within the desired size range (see column 4, lines 25-30). This disclosure of Bystrom anticipates claim 1.

Regarding claim 2, Bystrom discloses a homogeneous molecular mixture of a biologically active component and a lipid (carrier) (see column 2, lines 35-38). Bystrom is silent as to whether the pharmaceutically active ingredient is dispersed homogeneously in the pharmaceutically acceptable particulate carrier such that drug recovery from each of the plurality of samples taken from the medicament has a relative standard deviation from the mean of less than or equal to 5%. However, the examiner notes that a "homogeneous molecular mixture of a biologically active component and a lipid", as recited by Bystrom, would necessarily have sufficient homogeneity such that

drug recovery from each of a plurality of samples taken from the medicament has a relative standard deviation from the mean of less than or equal to 5%. This disclosure of Bystrom anticipates claim 2.

Regarding claims 3-5, the powder of Bystrom, having a diameter of less than 10 microns (see column 4, lines 20-24), is capable of passing through a sieve having a mesh of 50-3000 microns. This disclosure of Bystrom anticipates claims 3-5.

Regarding claim 6, Bystrom discloses inhalable medicaments (see Abstract). This disclosure of Bystrom anticipates claim 6.

Regarding claims 7 and 8, Bystrom discloses glucocorticosteroids as pharmaceutically active ingredients. Budesonide is mentioned as a preferred active ingredient (see column 3, line 53). This disclosure of Bystrom anticipates claims 7 and 8.

Regarding claims 9 and 10, Bystrom discloses lactose monohydrate as a preferred excipient (see column 4, lines 40-41). This disclosure of Bystrom anticipates claims 9 and 10.

Claims 1 and 3-5 are rejected under 35 U.S.C. 102(e) as being anticipated by Backstrom et al. (hereinafter "Backstrom").

Regarding claim 1, Backstrom discloses a process for preparing a medicament comprising combining a pharmaceutically active ingredient (insulin) in the form of an agglomerate of primary particles having an agglomerate particle size such that the agglomerate is capable of passing through a sieve having a mesh of 50-3000 microns

with a pharmaceutically acceptable carrier (enhancers) (see column 6, line 62 to column 7, line 2 and column 2, lines 32-59). The processes disclosed by Backstrom further include de-agglomerating the agglomerated by mechanical means such as a mixer (see column 3, lines 30-38)). In embodiments, at least 50%, preferably at least 90%, of the particles produced by the process of Backstrom have a diameter of up to 10 microns (see column 3, lines 30-35). This disclosure of Backstrom anticipates claim 1.

Regarding claims 3-5, Backstrom discloses the use of sieves having a slot width of 0.5 mm (see column 10, Examples 1 and 2). This disclosure of Backstrom anticipates claims 3-5.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2 is rejected under 35 U.S.C. 103 as being unpatentable over Bystrom et al.

Bystrom discloses homogeneous molecular mixtures of a pharmaceutically active ingredient and carrier (see column 2, lines 38-41). Bystrom is silent as to whether the pharmaceutically active ingredient is dispersed homogeneously in the pharmaceutically acceptable particulate carrier such that drug recovery from each of the plurality of

samples taken from the medicament has a relative standard deviation from the mean of less than or equal to 5%.

The Examiner maintains that although a "homogeneous molecular mixture" as recited by Bystrom would necessarily have sufficient homogeneity such that drug recovery from each of a plurality of samples taken from the medicament has a relative standard deviation from the mean of less than or equal to 5%, in the event that this limitation is not apparent in the teachings of Bystrom, it would have been well within the ordinary level of skill in the art at the time of the invention to arrive at the desired degree of homogeneity via routine experimentation. With regards to the limitation reciting the standard deviation from the mean, the examiner notes that generally, specific values will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating that such values are critical.

Response to Arguments

- **Claim Objections**

Applicants' amendments to claims 6 and 9 are acknowledged. With Applicants' amendments, the objections to claims 6 and 9 have been rendered moot.

- **Rejection under 35 U.S.C. § 102 in view of Walz**

Applicants argue that Walz does not disclose that its active ingredients are in the form of an agglomeration of primary particles, and that Walz does not disclose the

particle size of the active ingredient after the mixing step or that the mixing technique is such that the agglomerates of the active ingredient are broken up (see Applicants' Response at pages 4-5). Applicants' arguments pertaining to the rejection under 35 U.S.C. § 102 in view of Walz have been found persuasive, and this rejection has been withdrawn.

- **Rejection under 35 U.S.C. § 102 in view of Bystrom**

Applicants argue that Bystrom teaches an agglomeration containing both active agent and lipid, while step of (a) of claim 1 requires an agglomerate of the active ingredient only, which agglomerate is then mixed with the carrier (see Applicants' Response at page 5).

While Bystrom mentions agglomerations containing both active agent and lipid, as Applicants states, Bystrom contemplates mixing its agglomerated active ingredients with additives such as carriers such as crystalline lactose monohydrate (see column 4, lines 31-56).

Applicants admit that Bystrom discloses deagglomeration, but argue that the deagglomeration in Bystrom occurs in an inhalation device, while step (b) of claim 1 requires that the deagglomeration occurs in a mixer (see Applicants' Response at page 5).

The Examiner maintains that Bystrom anticipates step (b) of claim 1, because with the claims as written, "mixer" would read on an inhalation device or any device capable of mixing an agglomerate/carrier mixture to facilitate the formation of smaller

particles. Applicants define "mixer" in the specification as any conventional mixer capable of providing sufficient shear so that the mixed agglomerate is broken down (see paragraph [0025]). Given its broadest reasonable interpretation, a "mixer" as defined by the Applicants would include an inhalation device capable of breaking up agglomerates into smaller particles for inhalation via manual shaking of the user or the mixing of air with the agglomerates to provide shear.

Based on the reasons set forth above, the Examiner has maintained the rejection under 35 U.S.C. § 102 in view of Bystrom.

- **Rejection under 35 U.S.C. § 102 in view of Lizio**

Applicants argue that Lizio discloses neither a mixing step which breaks up agglomerated primary particles of active ingredient, nor any agglomeration of primary particles of active ingredient (see Applicants' Response at page 6). Applicants' arguments pertaining to the rejection under 35 U.S.C. § 102 in view of Lizio have been found persuasive, and this rejection has been withdrawn.

- **Rejection under 35 U.S.C. § 102 in view of Backstrom**

Applicants argue that the methods of Backstrom do not start with an agglomerate of active ingredient of defined size, nor does it include mixing of this agglomerate with a carrier and breaking up the agglomerate. Applicants further argue that Backstrom does not disclose the dispersion of active ingredient with the carrier having the particle sizes as recited in claim 1, and that the agglomerates of Backstrom pertain to an

agglomeration of active ingredient and carrier. Finally, Applicants argue that the deagglomeration in Backstrom is a deagglomeration which occurs in the inhalation device, and not deagglomeration in a mixer (see Applicants' Response at pages 7-8).

The Examiner disagrees with Applicants' assertions set forth above and reiterates that Backstrom anticipates at least claims 1 and 3-5. Firstly, Backstrom recites combining a pharmaceutically active ingredient in the form of an agglomerate of particles having an agglomerate particle size such that the agglomerate is capable of passing through a sieve having a mesh of 50-3000 μm with a pharmaceutically acceptable carrier (see column 8, lines 6-37; column 6, line 62 to column 7, line 2). At column 2, lines 32 to 58, Backstrom explicitly states combining an active compound in the form of agglomerated primary particles with a pharmaceutically acceptable carrier to form coarse particles having a diameter of 60-800 microns. Backstrom further states that its agglomerated primary particles may or may not contain pharmaceutically acceptable carriers (see column 3, lines 30-32). The agglomerates of Backstrom can be deagglomerated by any mechanical means, which a skilled artisan would interpret to include mixers, to yield a powder of which at least 50% consists of particles having a diameter of up to 10 microns (see column 3, lines 34-41). This particle size falls within Applicants' claimed size of 50 μm or less.

Based on the reasons set forth above, the Examiner has maintained the rejection under 35 U.S.C. § 102 in view of Backstrom.

- **Rejection under 35 U.S.C. § 103 in view of Walz, Bystrom or Lizio**

Applicants argue that the cited references fail to disclose an agglomerate of the ingredient prior to mixing with a carrier or a step of breaking up that agglomerate into primary particles dispersed in a pharmaceutically acceptable particulate carrier. Applicants then state that because these steps of claim 1 are not taught or suggested by the cited references, *prima facie* obviousness has not been established for claim 1 or dependent claim 2 (see Applicants' Response at pages 7-8).

Applicants' arguments pertaining to the rejections in view of Walz and Lizio have been found persuasive (see withdrawal of applicable 35 U.S.C. § 102rejections above). However, the rejection under 35 U.S.C. § 103 in view of Bystrom has been maintained. As mentioned above in the rejection under 35 U.S.C. § 102, Bystrom discloses a process for preparing a medicament comprising combining a pharmaceutically active ingredient in the form of an agglomerate of primary particles having an agglomerate particle size such that the agglomerate is capable of passing through a sieve having a mesh of 50-3000 microns with a pharmaceutically acceptable carrier. The processes disclosed in Bystrom further include deagglomerating the powder in a mixer to obtain particles within a respirable particle size range. The powder of Bystrom consists of particles having a diameter of less than 10 microns and at least 90% of the powder consists of particles within the desired size range. As stated above, the Examiner maintains that Bystrom anticipates step (b) of claim 1, because with the claims as written, "mixer" would read on an inhalation device or any device capable of mixing an agglomerate/carrier mixture to facilitate the formation of smaller particles.

Regarding the specific limitations of claim 2, the Examiner notes that Bystrom is silent as to whether the pharmaceutically active ingredient is dispersed homogeneously in the pharmaceutically acceptable particulate carrier such that drug recovery from each of the plurality of samples taken from the medicament has a relative standard deviation from the mean of less than or equal to 5%. However, the Examiner maintains that a "homogeneous molecular mixture" as recited by Bystrom would necessarily have sufficient homogeneity such that drug recovery from each of a plurality of samples taken from the medicament has a relative standard deviation from the mean of less than or equal to 5%. Furthermore, the Examiner maintains that it would have been well within the ordinary level of skill in the art at the time of the invention to arrive at the desired degree of homogeneity via routine experimentation.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RANDEEP SINGH whose telephone number is (571)270-3881. The examiner can normally be reached on Monday-Friday 10:00-6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571)272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Randeep Singh/
Examiner, Art Unit 1615

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